

IN THE UNITED STATES DISTRICT COURT  
FOR THE DISTRICT OF DELAWARE

IN RE: '318 PATENT  
INFRINGEMENT LITIGATION

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C.A. No. 05-356-KAJ  
(consolidated)

**NOTICE OF DEPOSITION AND SUBPOENA OF  
PFIZER, INC. PURSUANT TO  
FEDERAL RULE OF CIVIL PROCEDURE 45**

**PLEASE TAKE NOTICE** that, pursuant to Rule 45 of the Federal Rules of Civil Procedure, plaintiffs Janssen Pharmaceutica N.V., Janssen, L.P. and Synaptech, Inc. (collectively, "Janssen") will take the deposition upon oral examination of Pfizer, Inc., at the offices of Esquire Deposition Services, 216 E. 45<sup>th</sup> Street, 8<sup>th</sup> Fl., New York, NY 10017-3304, beginning at 10:00 A.M. on June 19, 2006.

NOTICE IS FURTHER GIVEN THAT the deposition will be recorded stenographically through instant visual display of testimony (real-time), by certified shorthand reporter and notary public or such other person authorized to administer oaths under the laws of the United States, and shall continue from day to day until completed. This deposition will be videotaped.

NOTICE IS FURTHER GIVEN THAT Pfizer, Inc. is instructed to produce documents, identified in the attached Subpoena, at the offices of Esquire Deposition Services, 216 E. 45<sup>th</sup> Street, 8<sup>th</sup> Fl., New York, NY 10017-3304 by 10:00 A.M. on June 12, 2006.

NOTICE IS FURTHER GIVEN THAT pursuant to the Federal Rules of Civil Procedure, Janssen will serve upon Pfizer, Inc. a Subpoena in a Civil Case. Attached hereto as Exhibit A is a true and correct copy of that Subpoena.

ASHBY & GEDDES

*/s/ Tiffany Geyer Lydon*

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Steven J. Balick (I.D. #2114)  
John G. Day (I.D. #2403)  
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Dated: May 22, 2006

169696.1

A088 Subpoena in a Civil Case

Issued by the  
**United States District Court**  
 SOUTHERN DISTRICT OF NEW YORK

IN RE: '318 PATENT INFRINGEMENT  
 LITIGATION

**SUBPOENA IN A CIVIL CASE**

Case Number:<sup>1</sup> C.A. No. 05-356-KAJ (consolidated)  
 (District of Delaware)

TO: Pfizer, Inc.  
 235 E. 42nd St.  
 New York, NY

- ☐ YOU ARE COMMANDED to appear in the United States District court at the place, date, and time specified below to testify in the above case.

PLACE OF TESTIMONY	COURTROOM
	DATE AND TIME

- ☒ YOU ARE COMMANDED to appear at the place, date, and time specified below to testify at the taking of a deposition in the above case. Please See Schedule A Attached

PLACE OF DEPOSITION Recording Method: By stenographer and videotape	DATE AND TIME
Esquire Deposition Services, 216 E. 45th Street, 8th FL, New York, New York 10017-3304	June 19, 2006 at 10:00 am


- ☒ YOU ARE COMMANDED to produce and permit inspection and copying of the following documents or objects at the place, date, and time specified below (list documents or objects): Please See Schedule B Attached

PLACE	DATE AND TIME
Esquire Deposition Services, 216 E. 45th Street, 8th FL, New York, New York 10017-3304	June 12, 2006 at 10:00 am

- ☐ YOU ARE COMMANDED to permit inspection of the following premises at the date and time specified below.

PREMISES	DATE AND TIME

Any organization not a party to this suit that is subpoenaed for the taking of a deposition shall designate one or more officers, directors, or managing agents, or other persons who consent to testify on its behalf, and may set forth, for each person designated, the matters on which the person will testify. Federal Rules of Civil Procedure, 30(b)(6).

ISSUING OFFICER'S SIGNATURE AND TITLE (INDICATE IF ATTORNEY FOR PLAINTIFF OR DEFENDANT) Attorney for Plaintiffs Janssen Pharmaceutica N.V., Janssen L.P., and Synaptech, Inc. 	DATE AND TIME May 22, 2006
ISSUING OFFICER'S NAME, ADDRESS AND PHONE NUMBER Tiffany Geyer Lydon, Esq. 222 Delaware Avenue, 17th Floor Wilmington, DE 19899 Tel: 302-654-1888	

(See Rule 45, Federal Rules of Civil Procedure, Parts C&D on next page)

<sup>1</sup> If action is pending in district other than district of issuance, state district under case number.

A088 Subpoena in a Civil Case

**PROOF OF SERVICE**

SERVED	DATE	PLACE
SERVED ON (PRINT NAME)	MANNER OF SERVICE	
SERVED BY (PRINT NAME)	TITLE	

**DECLARATION OF SERVER**

I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in the Proof of Service is true and correct.

Executed on

DATE

SIGNATURE OF SERVER

ADDRESS OF SERVER

**Rule 45, Federal Rules of Civil Procedure, Parts C&D****(c) PROTECTION OF PERSONS SUBJECT TO SUBPOENAS.**

(1) A party or an attorney responsible for the issuance and service of a subpoena shall take reasonable steps to avoid imposing undue burden or expense on a person subject to that subpoena. The court on behalf of which the subpoena was issued shall enforce this duty and impose upon the party or attorney in breach of this duty an appropriate sanction which may include, but is not limited to, lost earnings and reasonable attorney's fee.

(2)(A) A person commanded to produce and permit inspection and copying of designated books, papers, documents or tangible things, or inspection of premises need not appear in person at the place of production or inspection unless commanded to appear for deposition, hearing or trial.

(2)(B) Subject to paragraph (d)(2) of this rule, a person commanded to produce and permit inspection and copying may, within 14 days after service of subpoena or before the time specified for compliance if such time is less than 14 days after service, serve upon the party or attorney designated in the subpoena written objection to inspection or copying of any or all of the designated materials or of the premises. If objection is made, the party serving the subpoena shall not be entitled to inspect and copy materials or inspect the premises except pursuant to an order of the court by which the subpoena was issued. If objection has been made, the party serving the subpoena may, upon notice to the person commanded to produce, move at any time for an order to compel the production. Such an order to compel production shall protect any person who is not a party or an officer of a party from significant expense resulting from the inspection and copying commanded.

(3)(A) On timely motion, the court by which a subpoena was issued shall quash or modify the subpoena if it

(i) fails to allow reasonable time for compliance,

(ii) requires a person who is not a party or an officer of a party to travel to a place more than 100 miles from the place where that person resides, is employed or regularly transacts business in person, except that, subject to

the provisions of clause (c)(3)(B)(iii) of this rule, such a person may in order to attend trial be commanded to travel from any such place within the state in which the trial is held, or

(iii) requires disclosure of privileged or other protected matter and no exception or waiver applies, or

(iv) subjects a person to undue burden

(3)(B) If a subpoena

(i) requires disclosure of a trade secret or other confidential research, development, or commercial information, or

(ii) requires disclosure of an unretained expert's opinion or information not describing specific events or occurrences in dispute and resulting from the expert's study made not at the request of any party, or

(iii) requires a person who is not a party or an officer of a party to incur substantial expense to travel more than 100 miles to attend trial, the court may, to protect a person subject to or affected by the subpoena, quash or modify the subpoena, or, if the party in who behalf the subpoena is issued shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship and assures that the person to whom the subpoena is addressed will be reasonably compensated, the court may order appearance or production only upon specified conditions.

**(d) DUTIES IN RESPONDING TO SUBPOENA.**

(1) A person responding to a subpoena to produce documents shall produce them as they are kept in the usual course of business or shall organize and label them to correspond with the categories in the demand.

(2) When information subject to a subpoena is withheld on a claim that it is privileged or subject to protection as trial preparation materials, the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim.

4. “Person” and “persons” mean any natural person and any business, legal, corporate, or governmental entity, association, or organization.

5. “Alzheimer’s Disease” means any diagnosis, illness, or ailment described as being of the Alzheimer’s type, including without limitation Senile Dementia of the Alzheimer’s Type, and Alzheimer’s Dementia.

6. “318 patent” means United States Patent No. 4,663,318 attached hereto as Exhibit 1.

7. “Galantamine” includes without limitation galantamine, galanthamine, and any salt of galatamine, such as galantamine hydrobromide.

8. In these Requests, the present tense includes the past and future tenses, the connectives “and” and “or” shall be construed either disjunctively or conjunctively as necessary to bring within the scope of the Request all responses that might otherwise be construed to be outside of its scope, the singular shall include the plural and vice versa, “all” shall include “any” and vice versa, and “each” shall include “every” and vice versa, all to the end that each Request shall be construed to cover the broadest scope of information.

### **TOPICS**

1. Negotiations or communication between the Upjohn Company and Synaptech or Dr. Bonnie Davis regarding galantamine as a treatment for Alzheimer’s Disease.

2. The June 21, 1987, letter from Bonnie M. Davis to Dr. Alan Lemin, attached hereto as Exhibit 2.

3. The July 8, 1987, letter from Norman M. Pollack, Ph. D, attached hereto as Exhibit 3, including without limitation the meaning of, basis for, and any evaluation or

analysis concerning the statement set forth in the letter that “[a]lthough the use of galanthamine as a potential treatment for Alzheimer’s disease is scientifically interesting, I am afraid that we are not in a position to initiate licensing discussions concerning this therapeutic method.”

4. The September 15, 1987, letter from Norman M. Pollack, Ph. D, attached hereto as Exhibit 4, including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statement set forth in the letter that “we are already committed to other mechanistic approaches to Alzheimer’s disease which we consider more promising than that offered by galanthamine.”

5. Any evaluation or analysis conducted by or on behalf of the Upjohn Company concerning galantamine as a treatment for Alzheimer’s Disease.

## **SCHEDULE B**

Pursuant to Rule 45 of the Federal Rules of Civil Procedure, Plaintiffs Janssen Pharmaceutica N.V., Janssen, L.P., and Synaptech, Inc. hereby propound this subpoena on Pfizer, Inc. This subpoena calls for you to produce the documents described under the heading “Requests for Production of Documents” below, in accordance with the following “Definitions” and “Instructions.”

## **DEFINITIONS**

Notwithstanding any definition set forth below, each word, term, or phrase used in these Requests is intended to have the broadest meaning permitted under the Federal Rules of Civil Procedure. The following definitions and rules on construction apply to the Requests:

1. “Synaptech” shall mean Plaintiff Synaptech, Inc., Synaptec, Inc., and all of Synaptech, Inc., its corporate parents, corporate predecessors and past or present subsidiaries, affiliates, divisions, departments, officers, directors, principals, agents and employees including but not limited to Bonnie M. Davis, M.D.
2. “Dr. Bonnie Davis” refers to Bonnie M. Davis, M.D., holder of United States Patent No. 4,663,318.
3. “Document” means the complete original (or complete copy where the original is unavailable) and each non-identical copy (where different from the original because of notes made on the copy or otherwise) of any writing or record, including but not limited to all written, typewritten, handwritten, printed or graphic matter of any kind or nature, however produced or reproduced, any form of collected data for use with electronic data processing equipment, and any mechanical or electronic visual or sound recordings, including, without

limitation, all tapes and discs, now or formerly in your possession, custody or control, including all documents as defined in the broadest sense permitted by the Federal Rules of Civil Procedure. The term “document” includes, but is not limited to, e-mails, invoices, purchase orders, checks, receipts, letters and other correspondence, offers, contracts, agreements, bids, proposals, licenses, permits, reports to government agencies, ledgers, accounts receivable, accounts payable, account statements, financial statements, monthly reports, other reports, minutes of meetings, sales estimates, sales reports, memoranda, notes, calendar or diary entries, agendas, bulletins, graphs, charts, maps, photographs, drawings, surveys, data, price lists, summaries, telegrams, teletypes, computer printouts, magnetic tapes, discs, microfilm, and microfiche.

4. “Person” and “persons” mean any natural person and any business, legal, corporate, or governmental entity, association, or organization.

5. “Alzheimer’s Disease” means any diagnosis, illness, or ailment described as being of the Alzheimer’s type, including without limitation Senile Dementia of the Alzheimer’s Type, and Alzheimer’s Dementia.

6. “318 patent” means United States Patent No. 4,663,318 attached hereto as Exhibit 1.

7. “Galantamine” includes without limitation galantamine, galanthamine, and any salt of galatamine, such as galantamine hydrobromide.

8. In these Requests, the present tense includes the past and future tenses, the connectives “and” and “or” shall be construed either disjunctively or conjunctively as necessary to bring within the scope of the Request all responses that might otherwise be construed to be outside of its scope, the singular shall include the plural and vice versa, “all” shall include “any”



and vice versa, and “each” shall include “every” and vice versa, all to the end that each Request shall be construed to cover the broadest scope of information.

### **INSTRUCTIONS**

1. The response to each Request shall include all documents within your possession, custody, or control. The phrase “possession, custody, or control” means a document in your physical custody; or, that you own in whole or in part; or, have a right by contract, statute or otherwise to use, inspect, examine or copy on any terms; have an understanding, express or implied, that you may use, inspect, examine or copy on any terms; or you have, as a practical matter, the ability to use, inspect, examine or copy such document.

2. If any document or tangible thing that would have been responsive to the Requests below has been destroyed or is no longer in your possession, custody or control, you shall serve upon the undersigned counsel for the Plaintiff a written list that (i) identifies each such document by date, author or preparer, and addressee(s); and (ii) states the date of, and identity of the person responsible for, its destruction, loss, transfer, or other action by which the document or tangible thing left your possession, custody or control.

3. The response to each Request shall state, with respect to each item or category, that inspection and related activities will be permitted as requested, unless the Request is objected to, in which event the reasons for objection shall be stated. If objection is made to part of an item or category, the part shall be specified. Any such objection shall not extend the time within which you must otherwise answer or respond to a Request to which no specific objection has been made.

4. If you contend that an otherwise discoverable document would be excludable from production, state the reasons for such objection or grounds for exclusion and

identify each person having knowledge of the factual basis, if any, on which the objection or ground is asserted.

5. If any document that would have been responsive to any of the Requests below is not produced because of a claim of privilege or immunity, you shall serve upon the undersigned counsel for the Plaintiff a written list that (i) identifies each such document by date, author or preparer, and addressee(s); (ii) identifies the name and position of each person to whom a copy was furnished, and each person to whom the original or a copy was shown; (iii) states the general subject matter of each document; (iv) identifies the Request to which the withheld document is responsive; and (v) states the ground on which each document is asserted to be privileged or immune from disclosure. Any attachment to an allegedly privileged or immune document shall be produced unless you contend that the attachment is also privileged or immune, in which case the information specified in the previous sentence shall be separately provided for each such attachment.

6. If there is any question as to the meaning of any part of these Requests, or an issue as to whether production of responsive documents would impose an undue burden, counsel for the Plaintiff should be contacted promptly.

7. You may produce legible, complete, and exact copies of the original documents, provided that the originals be made available for inspection upon request by counsel for the Plaintiff.

8. You are requested to respond in writing to the following Requests, and produce the requested documents for inspection and copying, at the time, date, and location set forth in the subpoena.

**REQUESTS FOR PRODUCTION OF DOCUMENTS**

1. All documents concerning any evaluation, analysis, consideration, or discussion by the Upjohn Company of galantamine as a treatment for Alzheimer's Disease.
2. All documents concerning communications or discussions between the Upjohn Company and Synaptech or Dr. Bonnie Davis regarding the '318 patent.
3. All documents concerning communication between the Upjohn Company and Synaptech or Dr. Bonnie Davis regarding galantamine as a treatment for Alzheimer's Disease.
4. All documents concerning the June 21, 1987, letter from Bonnie M. Davis to Dr. Alan Lemin, attached hereto as Exhibit 2.
5. All documents concerning the July 8, 1987, letter from Norman M. Pollack, Ph. D, attached hereto as Exhibit 3, including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statement set forth in the letter that "[a]lthough the use of galanthamine as a potential treatment for Alzheimer's disease is scientifically interesting, I am afraid that we are not in a position to initiate licensing discussions concerning this therapeutic method."
6. All documents concerning the September 15, 1987, letter from Norman M. Pollack, Ph. D, attached hereto as Exhibit 4, including without limitation the meaning of, basis for, and any evaluation or analysis concerning the statement set forth in the letter that "we are already committed to other mechanistic approaches to Alzheimer's disease which we consider more promising than that offered by galanthamine."

# EXHIBIT 1

# United States Patent [19]

Davis

[11] Patent Number: 4,663,318

[45] Date of Patent: May 5, 1987

[54] METHOD OF TREATING ALZHEIMER'S DISEASE

[76] Inventor: Bonnie Davis, 17 Seacrest Dr.,  
Huntington, N.Y. 11743

[21] Appl. No.: 819,141

[22] Filed: Jan. 15, 1986

[51] Int. Cl. A61K 31/55

[52] U.S. Cl. 514/215

[58] Field of Search 514/215

[56] References Cited  
PUBLICATIONS

Chem. Abst. (81)-72615z (1974).

Chem. Abst. (86)-115157z (1977).

Horshenson et al. J. Med. Chem. vol. 29, No. 7, 7/86,  
pp. 1125-1130.

Kendall et al., J. Chem. & Hospital Pharmacol., (1985)  
10-327-330.

S. Chaplygina et al., J. of Highest Nervous Activity vol.  
XXIV 1976 Issue 5, pp. 1-4.

Krause, J. of Highest Nervous Activity, vol. XXII,  
1974, Issue 4.

Primary Examiner—Stanley J. Friedman  
Attorney, Agent, or Firm—Ladas & Parry

[57] ABSTRACT

Alzheimer's disease may be treated with galanthamine.

7 Claims, No Drawings

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## METHOD OF TREATING ALZHEIMER'S DISEASE

### GENERAL FIELD OF THE INVENTION

The present invention relates to a novel method of treating Alzheimer's disease and more particularly to a treatment using galanthamine.

### BACKGROUND ART

Galanthamine and acid addition salts thereof have, for many years, been known to have anticholinesterase properties. Cozanitis in *Anaesthesia* 29 163-8 (1974) describes the effect of galanthamine hydrobromide on plasma cortisol of patients receiving relaxant anaesthesia and Cozanitis et al in *Acta Anaesth. Scand.* 24:166-168 (1980) describe the effect of galanthamine on plasma ACTH values during anaesthesia. These studies showed an increase in both plasma cortisol and plasma ACTH when galanthamine was administered to patients together with atropine.

Ilyuchenok et al (Chemical Abstracts 70 36296K) describe the appearance of  $\theta$ -rhythm on an electroencephalogram when galanthamine is administered intravenously to rabbits.

Increase in short-term memory in dogs by use of galanthamine is described by Krauz in Chemical Abstracts 81 72615Z.

The antagonistic effect of galanthamine to scopolamine-induced amnesia in rats is described by Chaplygina et al in Chemical Abstracts 86 115157Z, and in *Zhurnal Vysshel Nervnoi Deiatelnosti imeni P. Pavlova (MOSKVA)* 26:1091-1093, 1976.

Alzheimer's disease, presenile dementia, causes much distress not only to those suffering from the disease, but also those who are close to them. The custodial care of advanced victims of the disease is a tremendous expense to society. At present, there is no effective means of improving the functional status of persons with the disease.

It is an object of the present invention to improve the cognitive function of patients with Alzheimer's disease.

### SUMMARY OF THE INVENTION

A method for treating Alzheimer's disease and related dementias which comprises administering to mammals, including humans, an effective Alzheimer's disease cognitively-enhancing amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof. A radioactively-labelled form of the molecule may also serve as a diagnostic test for Alzheimer's disease.

### DETAILED DESCRIPTION OF THE INVENTION

Galanthamine can be administered in any convenient chemical or physical form. For example, it may be administered as its hydrobromide, hydrochloride, methylsulfate or methiodide.

Galanthamine or its pharmaceutically-acceptable acid addition salts may be administered to a patient suffering from Alzheimer's disease orally or by subcutaneous or intravenous injection, or intracerebroventricularly by means of an implanted reservoir. It may be necessary to begin at lower doses than are ultimately effective.

Galanthamine and its acid addition salts form crystals. They are in general only sparingly soluble in water

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at room temperature and so injectible compositions are normally in the form of an aqueous suspension. If necessary, pharmaceutically-acceptable suspension aids may be employed. Typically, such a suspension will be employed at a concentration of 1-50 mg/ml more commonly 5-40 mg/ml, for example, 5-30 mg/ml or 10-40 mg/ml, typically 20-30 mg/ml of galanthamine. Typical dosage rates when administering galanthamine by injection are in the range 5-1,000 mg per day depending upon the patient. For example, divided doses in the range 0.5-5 mg/kg body weight per day may prove useful. Typically, one might administer a dosage of 50-300 mg per day to a patient of a body weight of 40-100 kg, although in appropriate cases such dosages may prove useful for patients having a body weight outside this range. In other cases, dosages as low as 10 mg and as high as 500 mg may be appropriate for persons in this body weight range.

Galanthamine or its pharmaceutically-acceptable acid addition salts may also be administered orally, for example, as an aqueous suspension or a solution in aqueous ethanol or as a solid such as a tablet or capsule. Suspensions or solutions for oral administration are typically of about the same concentration as those used for injections. However, it may be desirable when administering the drug orally to use a higher dosage rate than when administering it by injection. For example, dosages up to 2000 mg per day may be used, such as dosages in the range 100-600 mg per day. In preparing such tablets or capsules, standard tablet or capsulemaking techniques may be employed. The dosage rate of galanthamine or its pharmaceutically-acceptable salt will normally be in the same range as for oral administration of a liquid. If desired, a pharmaceutically-acceptable carrier such as starch or lactose may be used in preparing galanthamine tablets. Capsules may be prepared using soft galatine as the encapsulating agent. If desired, such capsules may be in the form of sustained release capsules wherein the main capsule contains microcapsules of galanthamine which release the contents over a period of several hours thereby maintaining a constant level of galanthamine in the patient's blood stream.

The following test provides a good animal model for Alzheimer's disease in humans: A selective lesion is placed in a subcortical nucleus (nucleus basalis of Meynert) with a resultant cortical cholinergic deficiency, similar in magnitude to that seen in early to moderate stage Alzheimer's disease. Numerous behavioral deficits, including the inability to learn and retain new information, characterizes this lesion. Drugs that can normalize these abnormalities would have a reasonable expectation of efficacy in Alzheimer's disease. Haroutunian, V, Kanof P, Davis, KL: Pharmacological alleviations of cholinergic-lesion-induced memory defects in rats. *Life Sciences* 37:945-952, 1985.

The following specific formulations may find use in treatment of Alzheimer's disease:

Tablets or capsules containing 5, 10 and 25 mg galanthamine hydrobromide to be taken four times a day, or a sustained-release preparation delivering an equivalent daily dose.

Parenteral solution containing 5 mg/ml.

Liquid formulation for oral administration available in 5 mg/5 ml and 25 mg/5 ml concentration.

There have been reports that galanthamine can cause cardiac arrhythmias. In such cases, it may be desirable to

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administer galanthamine in conjunction with another drug such as propanthelinbromide to control such arrhythmias.

I claim:

1. A method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

2. A method according to claim 1, wherein the administration is parenteral at a daily dosage of 5-1,000 mg of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

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3. A method according to claim 2, wherein said dosage rate is 50-300 mg per day.

4. A method according to claim 1, wherein said administration is oral and is in the range 10-2000 mg per day.

5. A method according to claim 4, wherein said dosage rate of 100-600 mg per day.

6. A method according to claim 1, wherein galanthamine is administered at a dosage rate of 0.1 to 4 mg/kg body weight of a patient, parenterally.

7. A method according to claim 1, wherein galanthamine is administered intracerebroventricularly via an implanted reservoir at a dosage rate of 0.01 to 5.0 mg/kg day.

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# **EXHIBIT 2**



REDACTED

17 Seacrest Drive  
Huntington, New York 11743  
June 21, 1987

Dr. Alan Lemin  
7298-26-2  
The Upjohn Company  
7000 Portage Road  
Kalamazoo, Michigan 49001

Dear Dr. Lemin,

Enclosed are a review of information on the use of galanthamine for the treatment of Alzheimer's disease, and several references.

You expressed an interest in animal data. Therefore, I would direct your attention to references 15, 17 and 18, all of which contain animal data demonstrating that galanthamine is a good central anticholinesterase. No. 15 (Tonkopii) is enclosed. It documents that galanthamine is equipotent to THA (tetrahydroaminoacridine). This is important because THA is the drug which was recently shown to have substantial clinical effects in Alzheimer's disease (Ref. 13). Ref. 15 also shows the time-course (page 1024) of the effect of galanthamine, administered peripherally, on the inhibition of brain acetylcholinesterase. A crude translation of Ref. 17 is enclosed. A scopolamine-induced amnesia, occurring in 60% of animals, was reversed in 60% of those animals by galanthamine injection (Table 1). Confirmation of galanthamine's reversal of anticholinergic dementia is found in Ref. 18 (Chem Abstract 105:218772m), which I have not had translated. You might also have access to Ref. 19, which demonstrates galanthamine's rapid localization to brain following oral administration. Thus, the literature indicates that galanthamine has the properties to reverse the cholinergic deficit in Alzheimer's disease. (Nevertheless, I'm not opposed to sending some for animal testing.)

Also enclosed is an article by Hollander et al, which is a bit of a review of the role of the cholinergic system in the pathophysiology and pharmacology of Alzheimer's disease.

I hope this information will be satisfactory. If you require anything further, please let me know. In any case, would you be kind enough to let me know that you have received this? Thank you. I look forward to hearing from you.

Yours truly,

Bonnie M. Davis, M.D.

Confidential

SYN RAZ-0000775

# EXHIBIT 3

# THE UPJOHN COMPANY

KALAMAZOO, MICHIGAN 49001, U.S.A.  
TELEPHONE (616) 323-4000

## PHARMACEUTICAL RESEARCH & DEVELOPMENT

NORMAN M. POLLACK, PH.D.  
Contract Consultant  
Research Contract Liaison

TELEPHONE: (616) 323-7400  
TELEX: 310-340140  
FACSIMILE: (616) 325-7372

July 8, 1987

Mr. John Richards  
Ladas & Parry  
26 West 61st Street  
New York, N.Y. 10023

Dear Mr. Richards:

We have completed our review of the information that we received from you and Dr. Davis. Although the use of galanthamine as a potential treatment for Alzheimer's disease is scientifically interesting, I am afraid that we are not in a position to initiate licensing discussions concerning this therapeutic method.

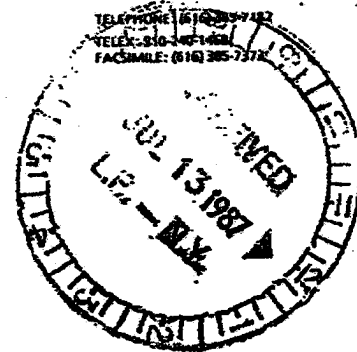
Our CNS pipeline is quite full at present, and each new opportunity must be measured against projects that are already underway. In the present case, we are unable to justify any diversion of resources from existing projects on the basis of the available information.

I do wish to thank you for bringing Dr. Davis' discovery to our attention.

Sincerely,

  
Norman M. Pollack

NMP:ejw



Confidential

SYN RAZ-0017577

# **EXHIBIT 4**

# THE UPJOHN COMPANY

KALAMAZOO, MICHIGAN 49001, U.S.A.  
TELEPHONE (616) 323-4000

## PHARMACEUTICAL RESEARCH & DEVELOPMENT

NORMAN M. POLLACK, Ph.D.  
Contract Consultant  
Research Contract (Amson)

TELEPHONE (616) 385-7182  
TELEX 910-240-5408  
FACSIMILE (616) 385-7373

September 15, 1987

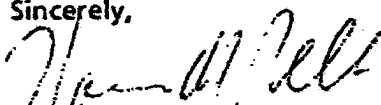
Bonnie M. Davis, M.D.  
17 Seacrest Drive  
Huntington, NY 11743

Dear Dr. Davis:

Thank you for your letter of July 13 and the additional information on the use of galanthamine in an animal model. This information has been reviewed with interest by our CNS Research Unit, but I am afraid that it has not prompted a reversal of our earlier conclusion, primarily because we are already fully committed to other mechanistic approaches to Alzheimer's disease which we consider more promising than that offered by galanthamine.

We do appreciate your interest in working with Upjohn, and we wish you success in your effort to find an industrial sponsor.

Sincerely,



Norman M. Pollack, Ph.D.

ejw

Confidential

SYN RAZ-0017576

**CERTIFICATE OF SERVICE**

I hereby certify that on the 22nd day of May, 2006, the attached **NOTICE OF DEPOSITION AND SUBPOENA OF PFIZER, INC. PURSUANT TO FEDERAL RULE OF CIVIL PROCEDURE 45** was served upon the below-named counsel of record at the address and in the manner indicated:

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*/s/ Tiffany Geyer Lydon*

\_\_\_\_\_  
Tiffany Geyer Lydon